

REMARKS

Claims 1-14, 16-27, and 29-40 constitute the pending claims in the present application. Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

Applicants have cancelled claims 1, 2, 3, 7, 28, 29, 37, and 38. Applicants have cancelled these claims solely to expedite prosecution. Applicants reserve the right to pursue these claims at a later date. Applicants have amended claim 4 by adding an element that the inhibitor is administered to the animal in an amount sufficient to treat Type II diabetes but not sufficient to suppress the immune system of the animal (support for this amendment is found on page 6 of the specification). Applicants reserve the right to pursue claims of similar or differing scope to the unamended claims at a later time. Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

1. Applicants acknowledge that a request for continued examination was granted, and that Applicants' submission filed on September 15, 2003 was entered.

2. Claims 2, 11, and 26 are objected to for having certain informalities. Applicants have corrected the informalities in the pending claim set in the following manner:

- a. Applicants have cancelled claim 2;
- b. the comma after "4" in claim 11, at line 1, has been deleted; and
- c. a comma has been inserted in claim 26, after the last chemical structure in the line.

The page numbers cited above are relative to the pages of Applicants' response filed September 15, 2003, and also correspond to the citations in the present Office Action.

Applicants submit that the aforementioned corrections do not narrow the scope of the amended claims. Applicants respectfully request reconsideration and removal of the objections in light of these corrections.

3. Claim 24 is objected to under 37 CFR 1.75(c) as being of improper dependent form. Applicants have corrected the dependency of the claim in the pending claim set. Applicants respectfully request reconsideration and removal of the objection in light of this amendment.
4. The specification is objected to for not providing proper antecedent basis for formula II in claim 28. Applicants have cancelled claim 28.
5. Claim 30 is provisionally rejected under 35 U.S.C. 101 for double patenting over claim 67 of co-pending Application No. 10/190,267. Applicants will address this rejection when it is no longer provisional.
6. Claims 1-14 and 16-40 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 38-42 and 46-68 of copending Application No. 09/628,255. Applicants have cancelled claims 1, 2, 3, 7, 28, 29, 37, and 38. For the remaining claims, Applicants will file a terminal disclaimer upon indication of claim allowance.
7. Claims 1-14 and 16-40 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 38-42 and 46-68 of copending Application No. 09/190,267. Applicants have cancelled claims 1, 2, 3, 7, 28, 29, 37, and 38. For the remaining claims, Applicants will file a terminal disclaimer upon indication of claim allowance.
8. Applicants acknowledge that the effective filing date of the instant claims 1-14 and 16-40 is deemed to be February 2, 1998, the filing date of provisional application 60/073,409. Applicants further favorably acknowledge that Deacon et al. (Diabetes, Vol. 47, pages 764-769) and WO Patent Application 98/25644 are no longer available as prior art against these claims. Applicants note with appreciation that Drucker, U.S. Pat. No. 5,952,301, is no longer applied against the instant claims because Drucker does not contain any disclosure concerning the use of dipeptidylpeptidase inhibitors.
9. Claims 1-3, 5-16, 20, 21, 25, and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application 95/153,309. Applicants assert that the rejection has been rendered moot because Applicants have cancelled claims 1, 2, 3, 7, and 29, and corrected

the dependencies of the remaining claims. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

10. Claims 1-3, 5-14, 16-24, 26, 27, 29-37, 39 and 40 are rejected under 35 U.S.C. 102(b) as being anticipated by the WO Patent Application '259. Applicants respectfully traverse the rejection to the extent it is maintained over the claims as amended.

With respect to claims 1, 2, 3, 7, 29, and 37, Applicants assert that the rejection has been rendered moot because Applicants have cancelled these claims. Furthermore, Applicants have corrected the dependencies of claims depending on claims 1, 2, 3, 7, 29, and 37.

Applicants also assert that the rejection of claims 30-36 has been rendered moot. Applicants have presently amended claim 30 to direct it to a method for treating Type II diabetes in an animal, comprising administering to the animal a composition including a boronyl peptidomimetic of a peptide selected from Pro-Pro, Ala-Pro, and (D)-Ala-(L)-Ala in an amount sufficient to treat the Type II diabetes, but not sufficient to suppress the immune system of the animal. Applicants assert that the '259 application does not anticipate claim 30, and claims dependent thereon, because it does not teach treating Type II diabetes in an animal by administering to the animal a composition including a sub-immunosuppressive amount of a boronyl peptidomimetic of Pro-Pro, Ala-Pro, or (D)-Ala-(L)-Ala.

In light of the amendments and cancellations described above, Applicants respectfully request reconsideration and withdrawal of the rejection.

11. Claims 1-13, 16, 20, 21, 25, and 38 are rejected under 35 U.S.C. 103(a) as being obvious over Balkan et al. abstract (Diabetologia, Suppl 40, A131 Abstract) in view of WO Patent Application 95/15309 and further in view of Efendic et al. (U.S. Patent No. 5,631,224). Applicants have cancelled claims 1, 2, 3, 7, and 38, and corrected the dependencies of the remaining rejected claims. Applicants respectfully traverse the rejection to the extent that it is maintained over the amended claims.

Claim 4 is the independent claim in the remaining rejected claim set. Claim 4 is directed to a method for treating Type II diabetes, comprising administering to an animal a composition including one or more inhibitors of dipeptidylpeptidase IV (DPIV) represented by Formula I in

an amount sufficient to treat Type II diabetes but not sufficient to suppress the immune system of the animal. The rejection is discussed below with respect to this claim.

Applicants point out that Balkan et al. is unavailable as prior art under 35 U.S.C. § 102(a) as set forth in the declaration under 37 C.F.R. § 1.131 filed herewith (Exhibit A). Because the claimed invention was made prior to the publication of Balkan et al., that reference is unavailable as prior art against the pending claims.

In the absence of Balkan et al., the '309 application does not render the instant claims obvious. The '309 application does not teach or suggest a method for treating Type II diabetes in an animal by administering sub-immunosuppressive doses of a DPIV inhibitor. Contrary to the Office Action's assertions, the '309 application does not give an enabling disclosure that teaches administering the compounds disclosed therein to an animal, let alone an animal with Type II diabetes.

The third reference the Office Action cited is not relevant to the pending claims because it only teaches administration of exogenous GLP-1 in order to treat Type II diabetes. None of Applicants' pending claims require administration of exogenous GLP-1. Furthermore, there is no teaching or suggestion that other compounds can be substituted for the exogenous GLP-1 disclosed in the reference.

Applicants further submit that the results of the instantly claimed methods are unexpected over any of the cited prior art. Applicants point out that DPIV inhibitors were known to have immunosuppressant activities (see, e.g., '309 application). Moreover, the use of highly potent and irreversible inhibitors, e.g., like the nanomolar DPIV inhibitors of the instant claims, was generally considered undesirable for antidiabetic agents (See Exhibit B: Pospisilik, J. A. et al., page 140, col. 1, lines 15-18). Thus, the fact that the instant claims are directed to methods for using these inhibitors for treating Type II diabetes at sub-immunosuppressive doses is an unexpected and non-obvious use of these compounds.

In light of the arguments presented above, Applicants respectfully request reconsideration and withdrawal of the rejection.

12. Claims 1-14, 16-24, 26, 27, and 29-40 are rejected under 35 U.S.C. 103(a) as being obvious over the Balkan et al. abstract, in view of the WO Patent Application 93/08259 and further in view of Efendic et al. Applicants have cancelled claims 1, 2, 3, 7, 29, and 37-38. Applicants have further corrected the dependencies of the remaining claims. Consequently, Applicants assert that the rejection is has been rendered moot with regards to these claims. Applicants respectfully traverse the rejection to the extent that it is maintained over the remaining amended claims on similar grounds as described in point 11 above.

Claims 4 and 30 are the independent claims in the rejected claim set. Claim 4 is directed to a method for treating Type II diabetes, comprising administering to an animal a composition including one or more inhibitors of dipeptidylpeptidase IV (DPIV) represented by Formula I in an amount sufficient to treat Type II diabetes but not sufficient to suppress the immune system of the animal. Applicants have presently amended claim 30 to direct it to a method for treating Type II diabetes in an animal, comprising administering to the animal a composition including a boronyl peptidomimetic of a peptide selected from Pro-Pro, Ala-Pro, and (D)-Ala-(L)-Ala in an amount sufficient to treat the Type II diabetes, but not sufficient to suppress the immune system of the animal. The rejection is discussed below with respect to these claims.

Applicants assert that the cited references, alone or in combination, do not teach or suggest all the elements of the present claims. As a threshold matter, Applicants note that the Office Action relied in part on Deacon et al. even though the Office Action had stated earlier that Deacon et al. is not available as prior art in view of Applicants earlier priority date. Accordingly, Applicants request that the several instances where the Office Action relied on Deacon et al. in making this obviousness rejection be withdrawn.

Applicant's argument for the non-obviousness of the rejected claims mirrors that which is presented in point 11 above. The only difference here is the import of the '259 patent application. Applicants assert that this application is insufficient to render the present claims obvious, even if the reference is combined Efendic et al. (Applicants refer the Examiner to arguments presented in point 11 above for discussion regarding Balkan et al. and Efendic et al.). The primary deficiency of the '259 application is that it does not teach or suggest administering the compounds disclosed therein at sub-immunosuppressive amounts to treat Type II diabetes.

Thus, the '259 application, alone or in combination with the other cited references, does not teach or suggest all the elements of the instant claims, and therefore does not render the claims obvious.

In light of the deficiencies in Balkan et al. and Efendic et al. that Applicants have already identified in point 11 above, and the reasons presented in the previous paragraph as to why the '259 application does not compensate for these deficiencies, Applicants assert that these references do not render the instant claims obvious. Accordingly, Applicants request reconsideration and withdrawal of this rejection.

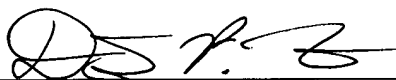
CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945**.

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Respectfully Submitted,



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